

WHAT IS CLAIMED IS:

1. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:

5 (a) the nucleotide sequence as set forth in either SEQ ID NO: 1 or SEQ ID NO: 3;

(b) the nucleotide sequence of the DNA insert in ATCC Deposit Nos. PTA-2665 or PTA-2666;

10 (c) a nucleotide sequence encoding the polypeptide as set forth in either SEQ ID NO: 2 or SEQ ID NO: 4;

(d) a nucleotide sequence that hybridizes under at least moderately stringent conditions to the complement of the nucleotide sequence of any of (a) - (c); and

(e) a nucleotide sequence complementary to the nucleotide sequence of any of (a) - (c).

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2. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:

20 (a) a nucleotide sequence encoding a polypeptide that is at least about 70 percent identical to the polypeptide as set forth in either SEQ ID NO: 2 or SEQ ID NO: 4, wherein the encoded polypeptide has an activity of the polypeptide set forth in either SEQ ID NO: 2 or SEQ ID NO: 4;

25 (b) a nucleotide sequence encoding an allelic variant or splice variant of the nucleotide sequence as set forth in either SEQ ID NO: 1 or SEQ ID NO: 3, the nucleotide sequence of the DNA insert in ATCC Deposit Nos. PTA-2665 or PTA-2666, or the nucleotide sequence of (a);

30 (c) a region of the nucleotide sequence of either SEQ ID NO: 1 or SEQ ID NO: 3, the nucleotide sequence of the DNA insert in ATCC Deposit Nos. PTA-2665 or PTA-2666, or the nucleotide sequence of (a) or (b) encoding a polypeptide fragment of at least about 25 amino acid residues, wherein the polypeptide fragment has an activity of the encoded polypeptide as set forth in either SEQ ID NO: 2 or SEQ ID NO: 4, or is antigenic;

(d) a region of the nucleotide sequence of either SEQ ID NO: 1 or SEQ ID NO: 3, the nucleotide sequence of the DNA insert in ATCC Deposit Nos. PTA-2665 or PTA-2666, or the nucleotide sequence of any of (a) - (c) comprising a fragment of at least about 16 nucleotides;

5 (e) a nucleotide sequence that hybridizes under at least moderately stringent conditions to the complement of the nucleotide sequence of any of (a) - (d); and

(f) a nucleotide sequence complementary to the nucleotide sequence of any of (a) - (d).

10 3. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:

(a) a nucleotide sequence encoding a polypeptide as set forth in either SEQ ID NO: 2 or SEQ ID NO: 4 with at least one conservative amino acid substitution, wherein the encoded polypeptide has an activity of the polypeptide set forth in either  
15 SEQ ID NO: 2 or SEQ ID NO: 4;

(b) a nucleotide sequence encoding a polypeptide as set forth in either SEQ ID NO: 2 or SEQ ID NO: 4 with at least one amino acid insertion, wherein the encoded polypeptide has an activity of the polypeptide set forth in either SEQ ID NO: 2 or SEQ ID NO: 4;

20 (c) a nucleotide sequence encoding a polypeptide as set forth in either SEQ ID NO: 2 or SEQ ID NO: 4 with at least one amino acid deletion, wherein the encoded polypeptide has an activity of the polypeptide set forth in either SEQ ID NO: 2 or SEQ ID NO: 4;

(d) a nucleotide sequence encoding a polypeptide as set forth in either SEQ ID NO: 2 or SEQ ID NO: 4 that has a C- and/or N- terminal truncation, wherein the encoded polypeptide has an activity of the polypeptide set forth in either SEQ ID NO: 2 or SEQ ID NO: 4;

25 (e) a nucleotide sequence encoding a polypeptide as set forth in either SEQ ID NO: 2 or SEQ ID NO: 4 with at least one modification selected from the group  
30 consisting of amino acid substitutions, amino acid insertions, amino acid deletions, C-

terminal truncation, and N-terminal truncation, wherein the encoded polypeptide has an activity of the polypeptide set forth in either SEQ ID NO: 2 or SEQ ID NO: 4;

(f) a nucleotide sequence of any of (a) - (e) comprising a fragment of at least about 16 nucleotides;

5 (g) a nucleotide sequence that hybridizes under at least moderately stringent conditions to the complement of the nucleotide sequence of any of (a) - (f); and

(h) a nucleotide sequence complementary to the nucleotide sequence of any of (a) - (e).

10 4. A vector comprising the nucleic acid molecule of any of Claims 1, 2, or 3.

5. A host cell comprising the vector of Claim 4.

6. The host cell of Claim 5 that is a eukaryotic cell.

15 7. The host cell of Claim 5 that is a prokaryotic cell.

8. A process of producing a TGF- $\beta$ -R polypeptide comprising culturing the host cell of Claim 5 under suitable conditions to express the polypeptide, and optionally  
20 isolating the polypeptide from the culture.

9. A polypeptide produced by the process of Claim 8.

10. The process of Claim 8, wherein the nucleic acid molecule comprises  
25 promoter DNA other than the promoter DNA for the native TGF- $\beta$ -R polypeptide operatively linked to the DNA encoding the TGF- $\beta$ -R polypeptide.

11. The isolated nucleic acid molecule according to Claim 2, wherein the percent identity is determined using a computer program selected from the group  
30 consisting of GAP, BLASTN, FASTA, BLASTA, BLASTX, BestFit, and the Smith-Waterman algorithm.

12. A process for determining whether a compound inhibits TGF- $\beta$ -R polypeptide activity or TGF- $\beta$ -R polypeptide production comprising exposing a cell according to any of Claims 5, 6, or 7 to the compound and measuring TGF- $\beta$ -R polypeptide activity or TGF- $\beta$ -R polypeptide production in said cell.

13. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence as set forth in either SEQ ID NO: 2 or SEQ ID NO: 4; and
- (b) the amino acid sequence encoded by the DNA insert in ATCC Deposit Nos. PTA-2665 or PTA-2666.

14. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of:

- (a) an amino acid sequence for an ortholog of either SEQ ID NO: 2 or SEQ ID NO: 4;
- (b) an amino acid sequence that is at least about 70 percent identical to the amino acid sequence of either SEQ ID NO: 2 or SEQ ID NO: 4, wherein the polypeptide has an activity of the polypeptide set forth in either SEQ ID NO: 2 or SEQ ID NO: 4;
- (c) a fragment of the amino acid sequence set forth in either SEQ ID NO: 2 or SEQ ID NO: 4 comprising at least about 25 amino acid residues, wherein the fragment has an activity of the polypeptide set forth in either SEQ ID NO: 2 or SEQ ID NO: 4, or is antigenic; and
- (d) an amino acid sequence for an allelic variant or splice variant of the amino acid sequence as set forth in either SEQ ID NO: 2 or SEQ ID NO: 4, the nucleotide sequence of the DNA insert in ATCC Deposit Nos. PTA-2665 or PTA-2666, or the amino acid sequence of either (a) or (b).

15. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence as set forth in either SEQ ID NO: 2 or SEQ ID NO: 4 with at least one conservative amino acid substitution, wherein the polypeptide has an activity of the polypeptide set forth in either SEQ ID NO: 2 or SEQ ID NO: 4;

5 (b) the amino acid sequence as set forth in either SEQ ID NO: 2 or SEQ ID NO: 4 with at least one amino acid insertion, wherein the polypeptide has an activity of the polypeptide set forth in either SEQ ID NO: 2 or SEQ ID NO: 4;

(c) the amino acid sequence as set forth in either SEQ ID NO: 2 or SEQ ID NO: 4 with at least one amino acid deletion, wherein the polypeptide has an activity of the polypeptide set forth in either SEQ ID NO: 2 or SEQ ID NO: 4;

10 (d) the amino acid sequence as set forth in either SEQ ID NO: 2 or SEQ ID NO: 4 that has a C- and/or N- terminal truncation, wherein the polypeptide has an activity of the polypeptide set forth in either SEQ ID NO: 2 or SEQ ID NO: 4; and

15 (e) the amino acid sequence as set forth in either SEQ ID NO: 2 or SEQ ID NO: 4 with at least one modification selected from the group consisting of amino acid substitutions, amino acid insertions, amino acid deletions, C-terminal truncation, and N-terminal truncation, wherein the polypeptide has an activity of the polypeptide set forth in either SEQ ID NO: 2 or SEQ ID NO: 4.

20 16. An isolated polypeptide encoded by the nucleic acid molecule of any of Claims 1, 2, or 3, wherein the polypeptide has an activity of the polypeptide set forth in either SEQ ID NO: 2 or SEQ ID NO: 4.

25 17. The isolated polypeptide according to Claim 14, wherein the percent identity is determined using a computer program selected from the group consisting of GAP, BLASTP, FASTA, BLASTA, BLASTX, BestFit, and the Smith-Waterman algorithm.

30 18. A selective binding agent or fragment thereof that specifically binds the polypeptide of any of Claims 13, 14, or 15.

19. The selective binding agent or fragment thereof of Claim 18 that specifically binds the polypeptide comprising the amino acid sequence as set forth in either SEQ ID NO: 2 or SEQ ID NO: 4, or a fragment thereof.

5           20. The selective binding agent of Claim 18 that is an antibody or fragment thereof.

21. The selective binding agent of Claim 18 that is a humanized antibody.

10           22. The selective binding agent of Claim 18 that is a human antibody or fragment thereof.

23. The selective binding agent of Claim 18 that is a polyclonal antibody or fragment thereof.

15           24. The selective binding agent Claim 18 that is a monoclonal antibody or fragment thereof.

20           25. The selective binding agent of Claim 18 that is a chimeric antibody or fragment thereof.

26. The selective binding agent of Claim 18 that is a CDR-grafted antibody or fragment thereof.

25           27. The selective binding agent of Claim 18 that is an antiidiotypic antibody or fragment thereof.

28. The selective binding agent of Claim 18 that is a variable region fragment.

30           29. The variable region fragment of Claim 28 that is a Fab or a Fab' fragment.

30. A selective binding agent or fragment thereof comprising at least one complementarity determining region with specificity for a polypeptide having the amino acid sequence of either SEQ ID NO: 2 or SEQ ID NO: 4.

5 31. The selective binding agent of Claim 18 that is bound to a detectable label.

32. The selective binding agent of Claim 18 that antagonizes TGF- $\beta$ -R polypeptide biological activity.

10 33. A method for treating, preventing, or ameliorating a TGF- $\beta$ -R polypeptide-related disease, condition, or disorder comprising administering to a patient an effective amount of a selective binding agent according to Claim 18.

15 34. A selective binding agent produced by immunizing an animal with a polypeptide comprising an amino acid sequence of either SEQ ID NO: 2 or SEQ ID NO: 4.

35. A hybridoma that produces a selective binding agent capable of binding a polypeptide according to any of Claims 13, 14, or 15.

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36. A method of detecting or quantitating the amount of TGF- $\beta$ -R polypeptide using the anti-TGF- $\beta$ -R antibody or fragment of Claim 18.

25 37. A kit for detecting or quantitating the amount of TGF- $\beta$ -R polypeptide in a biological sample, comprising the selective binding agent of Claim 18.

38. A composition comprising the polypeptide of any of Claims 13, 14, or 15, and a pharmaceutically acceptable formulation agent.

30 39. The composition of Claim 38, wherein the pharmaceutically acceptable formulation agent is a carrier, adjuvant, solubilizer, stabilizer, or anti-oxidant.

40. A polypeptide comprising a derivative of the polypeptide of any of Claims 13, 14, or 15.

5           41. The polypeptide of Claim 40 that is covalently modified with a water-soluble polymer.

10           42. The polypeptide of Claim 41, wherein the water-soluble polymer is selected from the group consisting of polyethylene glycol, monomethoxy-polyethylene glycol, dextran, cellulose, poly-(N-vinyl pyrrolidone) polyethylene glycol, propylene glycol homopolymers, polypropylene oxide/ethylene oxide co-polymers, polyoxyethylated polyols, and polyvinyl alcohol.

15           43. A composition comprising a nucleic acid molecule of any of Claims 1, 2, or 3 and a pharmaceutically acceptable formulation agent.

            44. The composition of Claim 43, wherein said nucleic acid molecule is contained in a viral vector.

20           45. A viral vector comprising a nucleic acid molecule of any of Claims 1, 2, or 3.

            46. A fusion polypeptide comprising the polypeptide of any of Claims 13, 14, or 15 fused to a heterologous amino acid sequence.

25           47. The fusion polypeptide of Claim 46, wherein the heterologous amino acid sequence is an IgG constant domain or fragment thereof.

30           48. A method for treating, preventing, or ameliorating a medical condition comprising administering to a patient the polypeptide of any of Claims 13, 14, or 15, or the polypeptide encoded by the nucleic acid of any of Claims 1, 2, or 3.

49. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:

5 (a) determining the presence or amount of expression of the polypeptide of any of Claims 13, 14, or 15, or the polypeptide encoded by the nucleic acid molecule of any of Claims 1, 2, or 3 in a sample; and

(b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide.

10 50. A device, comprising:

(a) a membrane suitable for implantation; and

(b) cells encapsulated within said membrane, wherein said cells secrete a protein of any of Claims 13, 14, or 15; and

15 said membrane is permeable to said protein and impermeable to materials detrimental to said cells.

51. A method of identifying a compound that binds to a TGF- $\beta$ -R polypeptide comprising:

20 (a) contacting the polypeptide of any of Claims 13, 14, or 15 with a compound; and

(b) determining the extent of binding of the TGF- $\beta$ -R polypeptide to the compound.

25 52. The method of Claim 51, further comprising determining the activity of the polypeptide when bound to the compound.

53. A method of modulating levels of a polypeptide in an animal comprising administering to the animal the nucleic acid molecule of any of Claims 1, 2, or 3.

30 54. A transgenic non-human mammal comprising the nucleic acid molecule of any of Claims 1, 2, or 3.

55. A process for determining whether a compound inhibits TGF- $\beta$ -R polypeptide activity or TGF- $\beta$ -R polypeptide production comprising exposing a transgenic mammal according to Claim 54 to the compound, and measuring TGF- $\beta$ -R polypeptide activity or TGF- $\beta$ -R polypeptide production in said mammal.

56. A nucleic acid molecule of any of Claims 1, 2, or 3 attached to a solid support.

10 57. An array of nucleic acid molecules comprising at least one nucleic acid molecule of any of Claims 1, 2, or 3.